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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,366	12/06/2000	Joshua S. Salafsky	0575/60934/JPW/ADM	8346

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EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

10

DATE MAILED: 10/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/731,366

Applicant(s)

SALAFSKY ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 29-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 33-37 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____

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DETAILED ACTION

Status of the claims

The amendment filed on August 12, 2002 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the claim positively recites that a second harmonic-active label is attached to the molecule and then further recites the absence of the second harmonic-active label. It is unclear if the second harmonic-active label is there or not. See also deficiencies found in claims 21 and 34.

Claim 36, line 1 "the molecule" is vague and indefinite. It is unclear which molecule applicant is referring to, the second molecule or the second harmonic-active labeled molecule.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1-4, 7, 8, 12, 13, 21, 23, 27, 28, and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Quinn et al (EP 0740156).

Quinn et al disclose the use of nonlinear optical methods of surface second-harmonic and sum-frequency generation to detect and quantify antibody-antigen interactions, polynucleotide hybridization and enzyme-substrate complexes (col 1, lines 7-11). Quinn et al disclose that antibodies, antigens, polynucleotides or enzymes are attached to a sensor surface (col 4, lines 1 and 2). Quinn et al disclose that a reporter molecule (label), which possess a molecular excitation close to 2f, may be attached by covalent or other means to the antibody, antigen, or enzyme thereby producing a condition of resonance enhancement (col 2, lines 46-57). Quinn et al disclose that the surface is into contact with a solution, which may contain the complementary species. Formation of a complex between the complementary species will result in a modification of the surface nonlinear optical properties. Measurement of the magnitude, angular dependence or any other parameter dependent on changes of nonlinear optical properties such as surface second-harmonic generation can be used to determine the amount of complex formation at the surface (col 4, lines 39-49).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 5, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Mattingly et al (US Patent 5,145,790).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the molecule being a pollutant.

Mattingly et al disclose specific binding reagents, such as antibodies, for detecting the presence or amount of polychlorinated biphenyls in a test sample (col 2, lines 10-34).

It would have been obvious to one of ordinary skill in the art to use the polychlorinated biphenyl specific antibodies taught by Mattingly et al in the method of Quinn et al because Quinn et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. antibody to detect the desired analyte, in this case polychlorinated biphenyls.

Claims 6, 11 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Marshall et al (US Patent 5,236,826).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose detecting analyte molecule on a surface of a nanoparticle or polymer bead. Quinn et al also fail to disclose a plurality of individual second harmonic-active labels bound together to increase the overall nonlinear susceptibility of the second harmonic-active moiety.

Marshall et al disclose the use beads or particles which have bound to their surface a molecule. These particles increase the surface area of the solid support and

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the use of these particles increase favorable reaction kinetics through Brownian motion, thereby establishing equilibrium faster than a system with less available surface for binding.

It would have been obvious to one of ordinary skill in the art to incorporate the use of particles as taught by Marshall et al into the method of Quinn et al because Marshall et al shows that these particles increase the surface area of the solid support and the use of these particles increase favorable reaction kinetics through Brownian motion, thereby establishing equilibrium faster than a system with less available surface for binding.

With respect to the plurality of individual second harmonic-active labels bound together in a fixed and determinate orientation with respect to each other so as to increase the overall nonlinear susceptibility of the second harmonic-active moiety as recited in the instant claims, the optimum overall nonlinear susceptibility of the second harmonic-active moiety can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation.” Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). “No invention is involved in discovering optimum ranges of a process by routine experimentation.” Id. At 458,105 USPQ at 236-237. The “discovery of an optimum value of a result effective variable in a known

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process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Buechler et al (US Patent 6,194,222).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the non-specific interaction being an electrostatic interaction.

Buechler et al disclose labels which are bound to the molecule by electrostatic interactions (col 21, lines 1-10). These interactions allow for an immunoassay system that is simple, rapid and reliable. Reliability in an immunoassay system is critical for the accurate measurement of the analyte (col 1, lines 40-43).

It would have been obvious to one of ordinary skill in the art to incorporate electrostatic interactions as taught by Buechler et al for the binding of the second harmonic-active moiety to the molecule of Quinn et al because Buechler et al shows that these interactions allow for an immunoassay system that is simple, rapid and reliable.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Wang et al (US Patent 5,696,157).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose that the second harmonic-active moiety is specific for an amine group.

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Wang et al disclose labels, which are specific for amine groups. These amine-reactive dyes are of particular relevance as they are commonly used to label proteins and polypeptides (col 13, lines 50-63). These labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component (col 1, lines 11-19).

It would have been obvious to one of ordinary skill in the art to substitute the label as taught by Wang et al for the label of Quinn et al because Wang et al shows that these amine labels are of particular relevance as they are commonly used to label proteins and polypeptide and that these labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component.

Furthermore, since the amine-specific dyes of Wang et al is within the chemical class as disclosed in the specification on page 16, line 24 (amine-specific dyes), it is considered that the amine-specific dye of Wang et al would be a second-harmonic active moiety.

Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Eisenthal et al (Photophysics of liquid Interfaces by Second Harmonic Spectroscopy, J.Phys. Chem 1996, 100, vol. 31, 12997-13006).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose an air-water interface and a water-glass interface.

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Eisenthal et al disclose the investigation of interface properties using second-harmonic spectroscopy. Eisenthal et al disclose studies of molecules at the silica/water interface and at the air/water interface. The study of molecules at these interfaces provides new information and insights into equilibrium and dynamic processes occurring at interfaces. These liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology (page 12998)

It would have been obvious to one of ordinary skill in the art to incorporate the interfaces as taught by Eisenthal et al into the method of Quinn et al because Eisenthal et al show that the study of molecules at these interfaces provide new information and insights into equilibrium and dynamic processes occurring at interfaces and that these liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Conboy et al (J. Chem. 1994, 98, 9688-9692).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to an oil-water interface.

Conboy et al disclose the investigation of oil-water interfaces. The study of this interface demonstrates the utility of using second harmonic generation to measure properties of the oil-water interface in the absence of any optical resonance's and expand the range of systems, which can be examined, by second harmonic generation (abstract and introduction). Conboy et al also disclose that there is a high interest in the

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characterization of oil-water interfaces because of the central role, which they play in many areas of chemistry, physics, and biology.

It would have been obvious to one of ordinary skill in the art to incorporate the oil-water interface as taught by Conboy et al into the method of Quinn et al because Conboy et al shows that the study of this interface demonstrates the utility of using second harmonic generation to measure properties of oil-water interface in the absence of any optical resonances and expand the range of systems which can be examined by second harmonic generation. Conboy et al also that there is a high interest in the characterization of oil-water interfaces because of the central role, which they play in many areas of chemistry, physics, and biology.

Claims 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Eisenthal et al (US 6055,051).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the interface is a cell surface.

Eisenthal et al disclose second harmonic generation and sum frequency generation used for surface analysis. Eisenthal et al disclose that the surface to be investigated can be a biological cell where the substance of interest at the surface of the cell (e.g. cell membrane) is detected. Eisenthal et al shows that the use of such a surface provide for an analytical tool for ascertaining whether or not the substance will adhere to cells, liposomes, emulsions and similar structures (col 4, line 57- col 5, line 5).

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It would have been obvious to one of ordinary skill in the art to incorporate services such as taught by Eisenthal et al into the method of Quinn et al because Eisenthal et al shows that the use of such a surface provide for an analytical tool for ascertaining whether or not the substance will adhere to cells, liposomes, emulsions and similar structures.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Tadano et al (US Patent 5,962,248).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the molecule being a chloride ion.

Tadano et al disclose a reagent for detecting chloride ions in a sample (col 1, line 66 – col 2, line 10).

It would have been obvious to one of ordinary skill in the art to use the enzyme substrate specific for chloride ions taught by Tadano et al in the method of Quinn et al because Quinn et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. enzyme substrate to detect the desired analyte, in this case chloride ion.

Response to Arguments

Applicant's arguments filed August 12, 2002 have been fully considered but they are not persuasive.

Applicant argues that Quinn et al do not anticipate the subject claimed invention because Quinn et al. do not disclose the use of a second harmonic-active label to detect

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a molecule at an interface or to detect a molecule in a medium, wherein the molecule is not detectable using the surface selective technique in the absence of the second-harmonic active label. This is not found persuasive because it is unclear from the recited claims if the second harmonic-active label is there or not. Therefore it is the Examiner's position that Quinn et al still reads on the claims as recited.

Applicant argues that the Mattingly et al reference fails to teach or suggest the use of a second harmonic-active label. This is not found persuasive because examiner has not relied upon the Mattingly et al reference for this limitation, but rather for the disclosure of specific binding reagents for detecting the presence or amount of pollutants.

Applicant argues that the Marshall et al reference does not teach or suggest the use of a second harmonic-active label. This is not found persuasive because examiner has not relied upon the Marshall et al reference for this limitation, but rather for the disclosure of detecting analyte molecule on a surface of a nanoparticle or polymer bead.

Applicant argues that the Buechler et al reference does not teach or suggest the use of a second harmonic-active label. This is not found persuasive because examiner has not relied upon the Buechler et al reference for this limitation, but rather for the disclosure of an electrostatic interaction.

Applicant argues that the Wang et al reference does not teach or suggest the use of a second harmonic-active label. This is not found persuasive because examiner has not relied upon the Buechler et al reference for this limitation, but rather for the disclosure of labels specific for amine groups.

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Applicant argues that the Eisenthal et al and Conboy et al references do not teach or suggest attaching a second harmonic-active label to a molecule in order to detect the molecule at an interface. This is not found persuasive because examiner has not relied upon these references for this limitation but rather for the disclosures of specific interfaces.

Applicant argues that the Tadano et al reference does not teach or suggest the use of a second harmonic-active label. This is not found persuasive because examiner has not relied upon the Tadano et al reference for this limitation, but rather for the limitation of a reagent for detecting chloride ions.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Nayfeh et al (US 6,456,423) disclose the use crystallized silicon nanoparticles as a biological marker for second harmonic imaging technique.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts
Examiner
Art Unit 1641
October 21, 2002



LONG V. LE
SUPERVISORY PATENT EXAMINER
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10/21/02